Electronic supplementary material

Article title: Remdesivir in the COVID-19 pandemic: an analysis of spontaneous reports in Vigibase during 2020

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Supplementary Table 1 – Proportion of ICSRs containing criteria for a severe or critical level of COVID-19 across the most commonly reported COVID-19-specific medicines

	Muscle Relax.	Gen. Anest.	Vasopressors	Blood subst.	Hypoxia/OSD	Severe	Tot N	|Diff to remdesivir|
Remdesivir	302 (6 %)	679 (13 %)	540 (10 %)	205 (4 %)	210 (4 %)	1089 (21 %)	5299	0
Ascorbic acid	61 (8 %)	107 (15 %)	93 (13 %)	50 (7 %)	24 (3 %)	172 (24 %)	720	3
Glucocorticoids	204 (7 %)	433 (15 %)	376 (13 %)	131 (5 %)	100 (4 %)	683 (24 %)	2814	3
Tocilizumab	70 (5 %)	124 (9 %)	120 (9 %)	41 (3 %)	42 (3 %)	214 (16 %)	1348	5
Zinc	49 (9 %)	97 (17 %)	78 (14 %)	46 (8 %)	26 (5 %)	150 (27 %)	560	6
Heparin group	314 (11 %)	625 (21 %)	489 (17 %)	188 (6 %)	91 (3 %)	869 (30 %)	2942	9
Azithromycin	116 (3 %)	259 (6 %)	247 (6 %)	84 (2 %)	57 (1 %)	442 (11 %)	4200	10
Hydroxychloroquine	89 (2 %)	165 (4 %)	174 (4 %)	36 (1 %)	51 (1 %)	326 (7 %)	4401	14
Lopinavir;Ritonavir	35 (2 %)	73 (4 %)	41 (2 %)	9 (1 %)	8 (0 %)	98 (6 %)	1656	15
Chloroquine	7 (1 %)	12 (2 %)	9 (2 %)	3 (1 %)	3 (1 %)	20 (4 %)	556	17
Ivermectin	2 (0 %)	5 (0 %)	6 (1 %)	2 (0 %)	6 (1 %)	14 (1 %)	1167	20
Total	309 (2 %)	414 (3 %)	878 (6 %)	248 (2 %)	737 (5 %)	1517 (10 %)	14574	11

Supplementary Table 1. *Percentages of severe COVID-19 ICSRs across COVID-19 medicines with at least 500 ICSRs. Note that one ICSR might contribute to several rows. Severe COVID-19 is defined as any reported medicine belonging to ATC-groups Muscle Relaxants (M03A), General anaesthetics (N01A), Adrenergic and Dopaminergic agents (C01CA, listed as "Vasopressors"), Sodium chloride or Albumin human (listed as Blood substitutes) or a reported reaction of Hypoxia or Oxygen Saturation Decreased (OSD), where the reported reaction is interpreted as COVID-19 symptoms. 'Severe' contains the number of ICSRs that fulfil at least one of the preceding criteria. Concomitant medicines are included in the counts. Note that heparin-like medicines and glucocorticoids are grouped. The grouping was made to achieve a concise view of the reporting concerning the ingoing substances with their well-established pre-COVID-19 use and a globally diverse substance use within the groups respectively.*

Supplementary Table 2 – Number of ICSRs for all COVID-19 specific medicine

Drug	N	%
Remdesivir	5149	35.4
Hydroxychloroquine	3731	25.7
Azithromycin	2894	19.9
Lopinavir;Ritonavir	1457	10.0
Ivermectin	1118	7.7
Tocilizumab	959	6.6
Glucocorticoids	798	5.5
Chloroquine	502	3.5
Favipiravir	450	3.1
Heparin group	449	3.1
Oseltamivir	322	2.2
Sarilumab	168	1.2
Ritonavir	94	0.6
Anakinra	71	0.5
Lopinavir	68	0.5
Ruxolitinib	64	0.4
Eculizumab	59	0.4
Umifenovir	53	0.4
Zinc	49	0.3
Ribavirin	45	0.3
Plasma	39	0.3
Ascorbic acid	37	0.3
Apixaban	36	0.2
Hyperimmune plasma Covid-19	36	0.2
Atazanavir	35	0.2
Darunavir	32	0.2
Interferon alfa-2b	30	0.2
Interferon beta	28	0.2
Tofacitinib	28	0.2
Interferon beta-1b	27	0.2

Drug	N	%
Colecalciferol	25	0.2
Rituximab	24	0.2
Baricitinib	23	0.2
Cobicistat;Darunavir	21	0.1
Interferon beta-1a	20	0.1
Itolizumab	20	0.1
Canakinumab	19	0.1
Immunoglobulin human normal	19	0.1
Interferon	19	0.1
Olokizumab	19	0.1
Rivaroxaban	19	0.1
Warfarin	19	0.1
Epoprostenol	16	0.1
Ciclosporin	15	0.1
Alteplase	14	0.1
Montelukast	13	0.1
Baloxavir marboxil	12	0.1
Colchicine	12	0.1
Ganciclovir	10	0.1
Aciclovir	9	0.1
Investigational drug	9	0.1
Apremilast	8	0.1
Immunoglobulins nos	7	0.0
Nitazoxanide	7	0.0
Valaciclovir	7	0.0
Mefloquine	6	0.0
Siltuximab	6	0.0
Thymalfasin	6	0.0

Supplementary Table 2*: Number of ICSRs per medicine, where the medicine is reported as suspected or interacting. As one ICSR may contain several medicines, rows are not mutually exclusive. Included in the list are all COVID-19 specific medicines (as describes in methods) with more than or equal to 5 ICSRs. Heparin-like medicines and glucocorticoids are grouped. The following COVID-19 specific medicines with between 1 and 4 ICSRs are omitted in the table: Acalabrutinib, Ademetionine, Allogenic mesenchymal stem cells nos, Almitrine, Aprotinin, Argatroban, Bcg vaccine, Beractant, Bevacizumab, Bromhexine, Calcium carbonate;Colecalciferol, Chlorine dioxide, Ciclesonide, Cobicistat, Conestat alfa, Daclatasvir, Darunavir;Ritonavir, Defibrotide, Ibrutinib, Icatibant, Iloprost, Infliximab, Inosine pranobex, Maraviroc, Narlaprevir, Nintedanib, Octreotide, Otilimab, Palmidrol, Peginterferon alfa-2a, Poractant alfa, Pyridostigmine, Riamilovir, Selinexor, Sofosbuvir, Vitamin D nos.*

Supplementary Table 3 – Most Frequent COVID-19 specific co-medications for remdesivir, ordered by ATC group

ATC level 2	ATC Name	Drug	N Report	% of Remdesivir
B01	Antithrombotic agents	Heparin group	1637	31
B01	Antithrombotic agents	Apixaban	87	2
B01	Antithrombotic agents	Epoprostenol	49	1
B01	Antithrombotic agents	Rivaroxaban	33	1
B01	Antithrombotic agents	Warfarin	27	1
B01	Antithrombotic agents	Alteplase	9	0
H02	Corticosteroids for systemic use	Glucocorticoids	1689	32
J01	Antibacterials for systemic use	Azithromycin	766	14
A11	Vitamins	Ascorbic acid	412	8
A11	Vitamins	Colecalciferol	192	4
L04	Immunosuppressants	Tocilizumab	355	7
L04	Immunosuppressants	Anakinra	20	0
L04	Immunosuppressants	Baricitinib	9	0
L04	Immunosuppressants	Apremilast	7	0
L04	Immunosuppressants	Sarilumab	6	0
A12	Mineral supplements	Zinc	327	6
A12	Mineral supplements	Calcium carbonate;Colecalciferol	5	0
P01	Antiprotozoals	Hydroxychloroquine	224	4
P01	Antiprotozoals	Chloroquine	5	0
R03	Drugs for obstructive airway diseases	Montelukast	54	1
R03	Drugs for obstructive airway diseases	Glucocorticoids	39	1
J05	Antivirals for systemic use	Lopinavir;Ritonavir	42	1
J05	Antivirals for systemic use	Aciclovir	15	0
J05	Antivirals for systemic use	Favipiravir	9	0
J05	Antivirals for systemic use	Oseltamivir	9	0
J05	Antivirals for systemic use	Valaciclovir	6	0
L01	Antineoplastic agents	Rituximab	10	0
L01	Antineoplastic agents	Selinexor	5	0

Supplementary Table 3. *Column '% of Remdesivir' displays the percentage of ICSRs with remdesivir that contained the specified co-medication. The following co-medications, grouped by ATC, were reported together with remdesivir on less than 5 ICSRs and are listed for completeness:*

Antithrombotic agents: Argatroban, Iloprost
Immunosuppressants: Ciclosporin, Eculizumab, Canakinumab, Siltuximab, Tofacitinib
Drugs for obstructive airway diseases: Ciclesonide
Antivirals for systemic use: Cobicistat;Darunavir, Ribavirin, Maraviroc, Atazanavir, Darunavir, Lopinavir, Ritonavir
Antineoplastic agents: Ibrutinib, Acalabrutinib, Ruxolitinib

Supplementary Table 4 – Most Frequent Non COVID-19 specific co-medications for remdesivir, ordered by ATC group

ATC level 2	ATC Name	Drug	N Report	% of Remdesivir
J01	Antithrombotic agents	Ceftriaxone	748	14
J01	Antithrombotic agents	Vancomycin	368	7
J01	Antithrombotic agents	Piperacillin;Tazobactam	357	7
J01	Antithrombotic agents	Cefepime	251	5
J01	Antithrombotic agents	Meropenem	162	3
J01	Antithrombotic agents	Doxycycline	152	3
J01	Antithrombotic agents	Levofloxacin	71	1
J01	Antithrombotic agents	Amoxicillin;Clavulanic acid	64	1
J01	Antithrombotic agents	Linezolid	57	1
J01	Antithrombotic agents	Metronidazole	51	1
J01	Antithrombotic agents	Clarithromycin	39	1
J01	Antithrombotic agents	Sulfamethoxazole;Trimethoprim	34	1
J01	Antithrombotic agents	Cefazolin	25	0
J01	Antithrombotic agents	Cefotaxime	24	0
J01	Antithrombotic agents	Ampicillin;Sulbactam	20	0
J01	Antithrombotic agents	Erythromycin	20	0
J01	Antithrombotic agents	Cefuroxime	14	0
J01	Antithrombotic agents	Aztreonam	12	0
J01	Antithrombotic agents	Ceftazidime	12	0
J01	Antithrombotic agents	Colistin	11	0
J01	Antithrombotic agents	Spiramycin	11	0
J01	Antithrombotic agents	Ciprofloxacin	10	0
J01	Antithrombotic agents	Daptomycin	9	0
J01	Antithrombotic agents	Tigecycline	8	0
J01	Antithrombotic agents	Amoxicillin	7	0
J01	Antithrombotic agents	Clindamycin	7	0
J01	Antithrombotic agents	Amikacin	6	0
J01	Antithrombotic agents	Ertapenem	6	0
J01	Antithrombotic agents	Teicoplanin	6	0
J01	Antithrombotic agents	Tobramycin	6	0
J01	Antithrombotic agents	Cefalexin	5	0
J01	Antithrombotic agents	Flucloxacillin	5	0
J01	Antithrombotic agents	Piperacillin	5	0
N02	Corticosteroids for systemic use	Paracetamol	702	13
N02	Corticosteroids for systemic use	Fentanyl	442	8
N02	Corticosteroids for systemic use	Acetylsalicylic acid	373	7
N02	Corticosteroids for systemic use	Morphine	132	2
N02	Corticosteroids for systemic use	Hydromorphone	95	2
N02	Corticosteroids for systemic use	Oxycodone	50	1
N02	Corticosteroids for systemic use	Metamizole	33	1
N02	Corticosteroids for systemic use	Tramadol	32	1
N02	Corticosteroids for systemic use	Clonidine	25	0
N02	Corticosteroids for systemic use	Oxycodone;Paracetamol	8	0
A02	Antibacterials for systemic use	Pantoprazole	467	9
A02	Antibacterials for systemic use	Famotidine	386	7
A02	Antibacterials for systemic use	Omeprazole	88	2
A02	Antibacterials for systemic use	Sodium bicarbonate	84	2
A02	Antibacterials for systemic use	Lansoprazole	42	1
A02	Antibacterials for systemic use	Esomeprazole	38	1
A02	Antibacterials for systemic use	Calcium carbonate	28	1
A02	Antibacterials for systemic use	Sucralfate	26	0
A02	Antibacterials for systemic use	Magnesium oxide	19	0
A02	Antibacterials for systemic use	Ranitidine	8	0
A02	Antibacterials for systemic use	Magnesium hydroxide	7	0
N05	Vitamins	Midazolam	335	6

Supplementary Table 4 (1/3) *Column '% of Remdesivir' displays the percentage of ICSRs with remdesivir that contained the specified co-medication. Co-medications, grouped by ATC, reported together with remdesivir on less than 5 ICSRs are listed below the third subtable, for completeness.*

N05	Vitamins	Dexmedetomidine	172	3
N05	Vitamins	Lorazepam	152	3
N05	Vitamins	Melatonin	138	3
N05	Vitamins	Quetiapine	67	1
N05	Vitamins	Alprazolam	31	1
N05	Vitamins	Hydroxyzine	29	1
N05	Vitamins	Haloperidol	27	1
N05	Vitamins	Olanzapine	18	0
N05	Vitamins	Buspirone	14	0
N05	Vitamins	Prochlorperazine	14	0
N05	Vitamins	Zolpidem	14	0
N05	Vitamins	Diazepam	13	0
N05	Vitamins	Risperidone	12	0
N05	Vitamins	Temazepam	11	0
N05	Vitamins	Aripiprazole	10	0
N05	Vitamins	Bromazepam	6	0
N01	Immunosuppressants	Propofol	497	9
N01	Immunosuppressants	Fentanyl	450	8
N01	Immunosuppressants	Ketamine	68	1
N01	Immunosuppressants	Etomidate	57	1
N01	Immunosuppressants	Lidocaine	38	1
N01	Immunosuppressants	Sufentanil	31	1
N01	Immunosuppressants	Remifentanil	21	0
N01	Immunosuppressants	Alfentanil	17	0
C01	Mineral supplements	Norepinephrine	481	9
C01	Mineral supplements	Amiodarone	125	2
C01	Mineral supplements	Epinephrine	61	1
C01	Mineral supplements	Phenylephrine	58	1
C01	Mineral supplements	Lidocaine	36	1
C01	Mineral supplements	Midodrine	32	1
C01	Mineral supplements	Digoxin	25	0
C01	Mineral supplements	Ibuprofen	24	0
C01	Mineral supplements	Dopamine	22	0
C01	Mineral supplements	Glyceryl trinitrate	20	0
C01	Mineral supplements	Isosorbide mononitrate	17	0
C01	Mineral supplements	Dobutamine	15	0
C01	Mineral supplements	Isosorbide dinitrate	5	0
V03	Antiprotozoals	Oxygen	567	11
V03	Antiprotozoals	Acetylcysteine	33	1
V03	Antiprotozoals	Naloxone	11	0
V03	Antiprotozoals	Sodium zirconium cyclosilicate	6	0
A10	Drugs for obstructive airway diseases	Insulin lispro	258	5
A10	Drugs for obstructive airway diseases	Insulin glargine	184	3
A10	Drugs for obstructive airway diseases	Insulin aspart	88	2
A10	Drugs for obstructive airway diseases	Insulin human	68	1
A10	Drugs for obstructive airway diseases	Metformin	58	1
A10	Drugs for obstructive airway diseases	Insulin porcine	56	1
A10	Drugs for obstructive airway diseases	Insulin detemir	44	1
A10	Drugs for obstructive airway diseases	Sitagliptin	12	0
A10	Drugs for obstructive airway diseases	Gliclazide	6	0
A10	Drugs for obstructive airway diseases	Empagliflozin	5	0
A10	Drugs for obstructive airway diseases	Glimepiride	5	0
A10	Drugs for obstructive airway diseases	Glipizide	5	0
A10	Drugs for obstructive airway diseases	Insulin bovine	5	0
A10	Drugs for obstructive airway diseases	Insulins and analogues	5	0
A10	Drugs for obstructive airway diseases	Linagliptin	5	0
A10	Drugs for obstructive airway diseases	Liraglutide	5	0
C03	Antivirals for systemic use	Furosemide	432	8
C03	Antivirals for systemic use	Bumetanide	33	1

Supplementary Table 4 (2/3) *Column '% of Remdesivir' displays the percentage of ICSRs with remdesivir that contained the specified co-medication. Co-medications, grouped by ATC, reported together with remdesivir in less than 5 ICSRs are listed below the third subtable, for completeness.*

C03	Antivirals for systemic use	Hydrochlorothiazide	30	1
C03	Antivirals for systemic use	Metolazone	27	1
C03	Antivirals for systemic use	Spironolactone	26	0
C03	Antivirals for systemic use	Torasemide	18	0
C03	Antivirals for systemic use	Chlorothiazide	7	0
C03	Antivirals for systemic use	Eplerenone	6	0
R03	Antineoplastic agents	Salbutamol	328	6
R03	Antineoplastic agents	Ipratropium	79	1
R03	Antineoplastic agents	Ipratropium;Salbutamol	65	1
R03	Antineoplastic agents	Epinephrine	61	1
R03	Antineoplastic agents	Budesonide	41	1
R03	Antineoplastic agents	Fluticasone	21	0
R03	Antineoplastic agents	Budesonide;Formoterol	20	0
R03	Antineoplastic agents	Fluticasone;Vilanterol	10	0
R03	Antineoplastic agents	Glycopyrronium	10	0
R03	Antineoplastic agents	Tiotropium	10	0
R03	Antineoplastic agents	Formoterol;Mometasone	8	0
R03	Antineoplastic agents	Mometasone	5	0
R03	Antineoplastic agents	Theophylline	5	0

Supplementary Table 4 (3/3*) *Column '% of Remdesivir' displays the percentage of ICSRs with remdesivir that contained the specified co-medication. The following co-medications, grouped by ATC, were reported together with remdesivir on less than 5 ICSRs and are listed below for completeness.*

Antibacterials for systemic use: Ampicillin, Avibactam;Ceftazidime, Tazobactam, Fosfomycin, Gentamicin, Moxifloxacin, Cefpodoxime, Ceftaroline fosamil, Cilastatin;Imipenem, Nafcillin, Phenoxymethylpenicillin, Bacitracin, Benzylpenicillin, Cefdinir, Cefixime, Ceftolozane;Tazobactam, Chloramphenicol, Lymecycline, Minocycline, Roxithromycin, Sultamicillin, Tetracycline

Analgesics: Pethidine, Piritramide, Sumatriptan, Buprenorphine, Codeine;Paracetamol, Dihydrocodeine, Eletriptan, Nefopam, Tapentadol

Drugs for acid related disorders: Aluminium hydroxide, Cimetidine, Dexlansoprazole, Misoprostol, Rabeprazole

Psycholeptics: Chlordiazepoxide, Clomethiazole, Hyoscine, Ramelteon, Chloral hydrate, Clozapine, Lormetazepam, Ziprasidone, Chlorpromazine, Lithium, Lurasidone, Oxazepam, Suvorexant, Zopiclone, Levomepromazine, Loxapine, Pimavanserin, Promazine, Zaleplon

Anesthetics: Benzocaine, Esketamine, Isoflurane, Sevoflurane, Bupivacaine, Dyclonine

Cardiac therapy: Ephedrine, Milrinone, Adenosine, Angiotensin ii, Dronedarone, Propafenone, Ranolazine, Flecainide, Metaraminol, Digitoxin, Indometacin, Isoprenaline, Procainamide, Ubidecarenone

All other therapeutic products: Sevelamer, Calcium acetate, Flumazenil, Folinic acid, Iodine, Iron, Phentolamine, Pralidoxime, Sugammadex

Drugs used in diabetes: Acarbose, Dapagliflozin, Repaglinide, Semaglutide, Alogliptin, Insulin degludec, Metformin;Sitagliptin, Tolbutamide

Diuretics: Bendroflumethiazide, Chlortalidone, Canrenoic acid, Etacrynic acid, Xipamide, Bendroflumethiazide;Potassium, Canrenone, Indapamide, Tolvaptan

Drugs for obstructive airway diseases: Ephedrine, Formoterol, Umeclidinium;Vilanterol, Fenoterol, Beclometasone;Formoterol;Glycopyrronium, Fenoterol;Ipratropium, Isoprenaline, Olodaterol;Tiotropium, Reproterol, Roflumilast, Umeclidinium

Supplementary Table 5 – Co-medications table

	Remdesivir	Tocilizumab	Hydroxychloroquine	Azithromycin	Heparin group
Total (S/I/C)	5299	1348	4401	4200	2942
Remdesivir		355	224	766	1670
Tocilizumab	355		470	364	351
Hydroxychloroquine	224	470		2024	846
Azithromycin	766	364	2024		983
Heparin group	1670	351	846	983	
Glucocorticoids	1697	353	605	907	1449
Lopinavir;Ritonavir	42	179	783	387	257
Ivermectin	17	10	75	456	45
Ascorbic acid	412	76	190	345	433
Zinc	329	54	120	276	333
Chloroquine	5	19	13	332	51
Aciclovir	15	8	16	8	15
Alteplase	9	10	8	11	17
Anakinra	20	16	39	31	25
Apixaban	87	13	45	24	57
Apremilast	7	6	2	4	8
Argatroban	3	4	2	3	5
Atazanavir	2		40	1	5
Baricitinib	9	1	7	6	12
Bromhexine	2	1	11	6	10
Calcium carbonate;Colecalciferol	5		5	3	3
Canakinumab	1		2		2
Ciclosporin	4	8	23	4	4
Cobicistat			7	2	
Cobicistat;Darunavir	4	6	30	13	7
Colchicine	23	11	22	16	19
Colecalciferol	192	30	61	153	190
Darunavir	2	7	30	7	18
Darunavir;Ritonavir			6		
Eculizumab	2	5	15	6	10
Epoprostenol	49	19	9	31	41
Favipiravir	9	15	106	77	93
Hyperimmune plasma Covid-19	10	1		2	1
Ibrutinib	4	4	8	6	1
Immunoglobulin human normal	6	10	12	8	8
Immunoglobulins nos	3	9	22	11	9
Interferon alfa-2b			1		
Interferon beta	4	8	22	11	4
Interferon beta-1b	1	8	40	18	13
Itolizumab			4	1	6
Lopinavir	2	4	42	12	5
Montelukast	54	6	6	27	41
Nitazoxanide		1	2	9	5
Oseltamivir	9	17	259	203	93
Plasma	91	28	29	45	67
Pyridostigmine	4	5	5	4	4
Ribavirin	4	16	26	27	10
Ritonavir	2	7	88	17	21
Rituximab	10	17	12	9	3
Rivaroxaban	33	6	15	16	13
Ruxolitinib	2	6	20	10	27
Sarilumab	6	4	86	68	62
Selinexor	5			2	5
Thymalfasin					
Umifenovir		1	2	2	5
Valaciclovir	6	1	4	2	8
Vitamin d nos	29	2	14	14	27
Warfarin	27	6	16	15	16
Other	2935	617	2115	2356	2549

Supplementary Table 5 (1/2): *Co-medication frequencies, for all medicines irrespective of medicine role (S/I/C = suspected, interacting or concomitant). Columns are all COVID-19 specific medicines (as described in methods) with more than 500 ICSRs, ordered with remdesivir and tocilizumab first, and then in descending order of total ICSRs. Rows are all COVID-19 specific medicines with at least one co-medication frequency of 5 with any of the column medicines, ordered as for the columns and then continuing alphabetically. Heparin-like medicines and glucocorticoids are grouped.* *This table continues on next page.*

	Glucocorticoids	Lopinavir;Ritonavir	Ivermectin	Ascorbic acid	Zinc	Chloroquine
Total (S/I/C)	2814	1656	1167	720	560	556
Remdesivir	1697	42	17	412	329	5
Tocilizumab	353	179	10	76	54	19
Hydroxychloroquine	605	783	75	190	120	13
Azithromycin	907	387	456	345	276	332
Heparin group	1449	257	45	433	333	51
Glucocorticoids		176	92	350	301	17
Lopinavir;Ritonavir	176		17	30	21	69
Ivermectin	92	17		14	10	2
Ascorbic acid	350	30	14		383	27
Zinc	301	21	10	383		11
Chloroquine	17	69	2	27	11	
Aciclovir	12	7		2	2	
Alteplase	8		1			
Anakinra	46	8		3	3	
Apixaban	75	11	2	16	22	1
Apremilast	6					
Argatroban	4				2	
Atazanavir	3	3		1		
Baricitinib	8	27				
Bromhexine	3			3	2	2
Calcium carbonate;Colecalciferol	4	2		2	1	
Canakinumab	5			2	1	
Ciclosporin	24	4				
Cobicistat		2				
Cobicistat;Darunavir	4	17	1	4		
Colchicine	21	3		7	8	
Colecalciferol	169	8	9	193	184	3
Darunavir	11	4		4		4
Darunavir;Ritonavir	3					
Eculizumab	3	3		3		
Epoprostenol	40	1		9	6	
Favipiravir	29	5	8	45	26	
Hyperimmune plasma Covid-19	2	18				
Ibrutinib	4				1	
Immunoglobulin human normal	9	3		1		
Immunoglobulins nos	12	7				
Interferon alfa-2b	8					
Interferon beta	11	25		1	1	
Interferon beta-1b	8	44		2	2	2
Itolizumab	5			4	2	
Lopinavir	22	1		3	1	1
Montelukast	50	6	2	15	23	
Nitazoxanide	9	8	3	1		
Oseltamivir	32	53	3	31	12	56
Plasma	74		4	28	28	1
Pyridostigmine	1				2	
Ribavirin	3	69		4	4	
Ritonavir	27	6		4	1	1
Rituximab	19	3				
Rivaroxaban	23	9	1	9	10	1
Ruxolitinib	21	13	3	1		1
Sarilumab	50	2	1	8	7	2
Selinexor	2			3	4	
Thymalfasin	6					
Umifenovir	12	7		1		
Valaciclovir	3	1				1
Vitamin d nos	28	1	1	25	15	1
Warfarin	19	6		7	7	
Other	2221	767	319	624	455	142

Supplementary table 5 (2/2)*: Co-medication frequencies for all medicines irrespectively of medicine role (S/I/C = suspected, interacting or concomitant). As columns are all COVID-19 specific medicines (as describes in methods) with more than 500 ICSRs, ordered with remdesivir and tocilizumab first, and then in descending order of total ICSRs. As rows are all COVID-19 specific medicines with at least one co-medication frequency of 5 with any of the column medicines, ordered as the columns and then continuing alphabetically. Heparin-like medicines and glucocorticoids are grouped. This table is a continuation from the previous page.*

Supplementary Table 6 – Reported PTs for remdesivir

PT	N	%
Alanine aminotransferase increased	830	16.1
Aspartate aminotransferase increased	503	9.8
Acute kidney injury	423	8.2
Death	410	8.0
Liver function test increased	349	6.8
Blood creatinine increased	282	5.5
Bradycardia	237	4.6
Transaminases increased	208	4.0
Drug ineffective	194	3.8
Respiratory failure	172	3.3
Therapy cessation	158	3.1
Hypotension	153	3.0
Cardiac arrest	149	2.9
Hepatic enzyme increased	140	2.7
Off label use	139	2.7
Hypoxia	129	2.5
Nausea	120	2.3
Renal impairment	115	2.2
Adverse event	109	2.1
Dyspnoea	103	2.0
Glomerular filtration rate decreased	100	1.9
COVID-19	93	1.8
Condition aggravated	92	1.8
Therapy interrupted	90	1.7
Oxygen saturation decreased	88	1.7
Rash	78	1.5
Renal failure	77	1.5
Septic shock	77	1.5
Acute respiratory failure	70	1.4
General physical health deterioration	70	1.4
Acute respiratory distress syndrome	67	1.3
Infusion site extravasation	64	1.2
Blood alkaline phosphatase increased	62	1.2
Product preparation error	62	1.2
Pyrexia	61	1.2
Atrial fibrillation	60	1.2
Blood bilirubin increased	60	1.2
Heart rate decreased	58	1.1
Cardio-respiratory arrest	56	1.1
Infusion related reaction	56	1.1
Multiple organ dysfunction syndrome	54	1.0
COVID-19 pneumonia	53	1.0
Pulseless electrical activity	52	1.0
Vomiting	50	1.0
Haemodialysis	49	1.0
Product use issue	49	1.0
International normalised ratio increased	47	0.9
Shock	47	0.9
Chills	46	0.9
Pneumonia	46	0.9
Sepsis	46	0.9
Hypertransaminasaemia	44	0.9
COVID-19 treatment	43	0.8
Tachycardia	40	0.8
Respiratory distress	38	0.7
Sinus bradycardia	35	0.7
Dialysis	34	0.7
Hyperhidrosis	34	0.7
Diarrhoea	33	0.6
Creatinine renal clearance decreased	32	0.6
Extravasation	32	0.6
Hypertension	31	0.6
Respiratory disorder	31	0.6
Product preparation issue	30	0.6
Hyperkalaemia	29	0.6

PT	N	%
Maternal exposure during pregnancy	29	0.6
Product storage error	29	0.6
Pulmonary embolism	28	0.5
Product administration error	27	0.5
Product dose omission issue	26	0.5
Product use in unapproved indication	26	0.5
SARS-CoV-2 test positive	26	0.5
Acute myocardial infarction	25	0.5
Chest pain	25	0.5
Blood urea increased	24	0.5
Disseminated intravascular coagulation	24	0.5
Exposure during pregnancy	24	0.5
Pruritus	24	0.5
Disease progression	23	0.4
Hepatotoxicity	23	0.4
Pulse absent	23	0.4
Anxiety	22	0.4
Seizure	22	0.4
Thrombocytopenia	22	0.4
Unresponsive to stimuli	22	0.4
Blood pressure decreased	21	0.4
Clinical trial participant	21	0.4
Incorrect dose administered	21	0.4
Ischaemic hepatitis	21	0.4
Metabolic acidosis	21	0.4
Renal tubular necrosis	21	0.4
Tachypnoea	21	0.4
Ventricular tachycardia	21	0.4
Acidosis	20	0.4
Cough	20	0.4
Disease complication	20	0.4
Erythema	20	0.4
Flushing	20	0.4
Foetal exposure during pregnancy	20	0.4
Haemoglobin decreased	20	0.4
Hepatitis	20	0.4
Hyperglycaemia	20	0.4
Liver function test abnormal	20	0.4
Pneumothorax	20	0.4
Shock haemorrhagic	20	0.4
Agitation	19	0.4
Dizziness	19	0.4
Headache	19	0.4
Malaise	19	0.4
Mental status changes	19	0.4
Product dispensing error	19	0.4
Respiratory arrest	19	0.4
Blood creatine increased	18	0.3
Electrocardiogram QT prolonged	18	0.3
Gastrointestinal haemorrhage	18	0.3
Hepatic failure	18	0.3
Anaemia	17	0.3
Liver injury	17	0.3
Medication error	17	0.3
Palliative care	17	0.3
Swelling	17	0.3
White blood cell count increased	17	0.3
Confusional state	16	0.3
Fibrin D dimer increased	16	0.3
Hepatocellular injury	16	0.3
Platelet count decreased	16	0.3
Asthenia	15	0.3
Cerebrovascular accident	15	0.3
Intentional product use issue	15	0.3
Premature delivery	15	0.3

Supplementary Table 6 (1/3)*: Number of ICSRs with each PT for remdesivir, where remdesivir is reported as suspected or interacting. As one ICSR may contain several reactions, rows are not mutually exclusive. Included in the list are all PTs with at least 5 ICSRs. This table continues on next page.*

PT	N	%
Rash maculo-papular	15	0.3
Blood lactate dehydrogenase increased	14	0.3
Chest discomfort	14	0.3
Infusion site swelling	14	0.3
Urticaria	14	0.3
Acute hepatic failure	13	0.3
Fatigue	13	0.3
Heart rate increased	13	0.3
Premature baby	13	0.3
Tremor	13	0.3
Urine output decreased	13	0.3
Angioedema	12	0.2
Anuria	12	0.2
Blood creatine phosphokinase increased	12	0.2
Hospice care	12	0.2
Inappropriate schedule of product administration	12	0.2
Inflammatory marker increased	12	0.2
Lactic acidosis	12	0.2
Lethargy	12	0.2
Oliguria	12	0.2
Pneumonia bacterial	12	0.2
Rash erythematous	12	0.2
Ventricular fibrillation	12	0.2
Blood glucose increased	11	0.2
Blood pressure increased	11	0.2
Body temperature increased	11	0.2
Cytokine storm	11	0.2
Delirium	11	0.2
Drug-induced liver injury	11	0.2
Dysphagia	11	0.2
Encephalopathy	11	0.2
Endotracheal intubation	11	0.2
Feeling hot	11	0.2
Gamma-glutamyltransferase increased	11	0.2
Hepatic function abnormal	11	0.2
Hypersensitivity	11	0.2
Infusion site erythema	11	0.2
Leukocytosis	11	0.2
Liver disorder	11	0.2
Nephropathy toxic	11	0.2
Pain	11	0.2
Platelet count increased	11	0.2
Respiratory acidosis	11	0.2
Abdominal pain upper	10	0.2
Bacteraemia	10	0.2
Blood calcium decreased	10	0.2
Cardiac failure	10	0.2
Hypercapnia	10	0.2
Lung infiltration	10	0.2
Oxygen consumption increased	10	0.2
Peripheral swelling	10	0.2
Pneumonia pseudomonal	10	0.2
Prothrombin time prolonged	10	0.2
Retroperitoneal haemorrhage	10	0.2
Troponin increased	10	0.2
White blood cell count decreased	10	0.2
Arrhythmia	9	0.2
Blood albumin decreased	9	0.2
C-reactive protein increased	9	0.2
Cholestasis	9	0.2
Depressed level of consciousness	9	0.2
Feeling abnormal	9	0.2
Haemodynamic instability	9	0.2
Hypernatraemia	9	0.2
Pancreatitis	9	0.2
Supraventricular tachycardia	9	0.2
Blood lactic acid increased	8	0.2
Blood potassium increased	8	0.2
Coagulopathy	8	0.2
Continuous haemodiafiltration	8	0.2
Drug interaction	8	0.2
Extra dose administered	8	0.2
Fluid overload	8	0.2
Glomerular filtration rate increased	8	0.2
Haematocrit decreased	8	0.2
Hypokalaemia	8	0.2
Hypovolaemic shock	8	0.2
Intra-abdominal haemorrhage	8	0.2
Low birth weight baby	8	0.2
Overdose	8	0.2
Pneumonia staphylococcal	8	0.2
Procalcitonin increased	8	0.2
Pulmonary oedema	8	0.2
Rash papular	8	0.2
Rash pruritic	8	0.2
Renal injury	8	0.2
Serum ferritin increased	8	0.2
Subcutaneous emphysema	8	0.2
Transfusion	8	0.2
Abdominal pain	7	0.1
Administration site extravasation	7	0.1
Bacterial infection	7	0.1
Blood magnesium increased	7	0.1
Brain death	7	0.1
Burning sensation	7	0.1
Dehydration	7	0.1
Eye irritation	7	0.1
Hypoaesthesia	7	0.1
Infusion site oedema	7	0.1
Intercepted product preparation error	7	0.1
Paralysis	7	0.1
Red blood cell count decreased	7	0.1
Refusal of treatment by patient	7	0.1
Rhabdomyolysis	7	0.1
Somnolence	7	0.1
Transcription medication error	7	0.1
Abdominal distension	6	0.1
Alanine aminotransferase abnormal	6	0.1
Anaphylactic reaction	6	0.1
Azotaemia	6	0.1
Bilevel positive airway pressure	6	0.1
Blood pressure systolic decreased	6	0.1
Cardiogenic shock	6	0.1
Cerebral infarction	6	0.1
Chest X-ray abnormal	6	0.1
Cholelithiasis	6	0.1
Creatinine renal clearance increased	6	0.1
Decreased appetite	6	0.1
Drug eruption	6	0.1
Epistaxis	6	0.1
Hepatic steatosis	6	0.1
Hyperbilirubinaemia	6	0.1
Hyponatraemia	6	0.1
Infusion site pain	6	0.1
Injection site extravasation	6	0.1
Intentional dose omission	6	0.1
Iron deficiency	6	0.1
Mechanical ventilation	6	0.1
Oedema	6	0.1
Paraesthesia	6	0.1

Supplementary Table 6 (2/3): *Number of ICSRs with each PT for remdesivir, where remdesivir is reported as suspected or interacting. As one ICSR may contain several reactions, rows are not mutually exclusive. Included in the list are all PTs with at least 5 ICSRs. This table continues on next page.*

PT	N	%
Pneumomediastinum	6	0.1
Pneumonia viral	6	0.1
Pulmonary function test decreased	6	0.1
Respiratory rate increased	6	0.1
Retroperitoneal haematoma	6	0.1
Urinary tract infection	6	0.1
Ventricular extrasystoles	6	0.1
Wrong product administered	6	0.1
Wrong technique in product usage process	6	0.1
Accidental exposure to product	5	0.1
Ammonia increased	5	0.1
Aphasia	5	0.1
Blood culture positive	5	0.1
Brain injury	5	0.1
Caesarean section	5	0.1
Carotid artery stenosis	5	0.1
Constipation	5	0.1
Critical illness	5	0.1
Haematuria	5	0.1
Hallucination	5	0.1
Heparin-induced thrombocytopenia	5	0.1
Hyperlipidaemia	5	0.1
Hypothermia	5	0.1
Hypovolaemia	5	0.1
Incorrect product administration duration	5	0.1
Intercepted product dispensing error	5	0.1
Lacrimation increased	5	0.1
Myalgia	5	0.1
Neutrophil count increased	5	0.1
Palpitations	5	0.1
Paravenous drug administration	5	0.1
Rash macular	5	0.1
Renal replacement therapy	5	0.1
Staphylococcal infection	5	0.1
Swelling face	5	0.1
Thrombophlebitis	5	0.1
Unevaluable event	5	0.1
Wheezing	5	0.1

Supplementary Table 6 (3/3)*: Number of ICSRs with each PT for remdesivir, where remdesivir is reported as suspected or interacting. As one ICSR may contain several reactions, rows are not mutually exclusive. Included in the list are all PTs with at least 5 ICSRs. This table is a continuation from the previous page.*

Supplementary Table 7 – PTs omitted from Figure 4

Adverse event
Coronavirus infection
COVID-19
COVID-19 treatment
COVID-19 pneumonia
Exposure during pregnancy
Infusion site extravasation
Intentional product use issue
Maternal exposure during pregnancy
No adverse event
Off label use
Product use in unapproved indication
Product use issue
SARS-CoV-2 test positive

Supplementary table 7*: PTs listed are omitted from Figure 4.*